Postarrest Interventions that Save Lives

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KEYWORDS

• Percutaneous coronary intervention • Temperature-targeted management • Seizure
• Mechanical circulatory support

KEY POINTS

- A focused diagnostic work-up to identify and reverse the inciting cause of arrest is essential to prevent rearrest and improve outcomes.
- Percutaneous coronary intervention should be considered for all patients after arrest.
- Preventing secondary brain injury by initiating targeted temperature management, maintaining optimal perfusion pressure, optimizing ventilator management, and controlling seizures can further improve outcomes.
- Transfer to specialty care should be considered during initial resuscitation efforts.
- Neurologic prognostication and withdrawal of life-sustaining therapy for perceived poor neurologic prognosis should be delayed in all cases.

INTRODUCTION

Care of patients resuscitated from cardiac arrest is challenging. Mortality and morbidity are common even after return of spontaneous circulation (ROSC). In managing these patients, clinicians must simultaneously address multiple problems. Goals in the early postarrest period include cardiopulmonary stabilization and prevention of secondary brain injury. Given the complexity and importance of the minutes immediately after ROSC, an organized approach is crucial and is associated with demonstrable outcome benefits.[1]

Identifying Causes of Arrest that Require Immediate Intervention

Autopsy series show cardiac causes, particularly coronary artery disease, are the most common cause of out-of-hospital cardiac arrest (OHCA).[2] However, only a minority of patients with OHCA are successfully resuscitated and survive to hospital

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care. The demographics of the subgroup seen and evaluated in the emergency department (ED) are distinct from the broader group of patients with OHCA.[3] A recent large cohort study classified the arrest cause after a full inpatient diagnostic work-up, finding only a minority of cases were caused by acute coronary syndrome (ACS) or other cardiac causes.[4] A rapid, directed work-up is needed to evaluate for treatable arrest causes (**Table 1**). A brief history should be obtained from emergency medical services or family regarding the circumstances of the arrest. In some cases, history may suggest the underlying cause (eg, antecedent chest pain followed by ventricular fibrillation may suggest ACS, whereas presence of drug paraphernalia at the scene may suggest overdose). A focused physical examination can evaluate for signs of trauma, gastrointestinal hemorrhage, primary neurologic catastrophes such as intracerebral hemorrhage, and so forth.

Table 1
Diagnostic evaluation of patients after cardiac arrest

Underlying Cause	Work-up
Cardiac • ACS • Structural heart disease • Cardiomyopathies • RV failure (eg, pulmonary hypertension, pulmonary embolus) • Arrhythmia	ECG Troponin BNP Point-of-care ultrasonography CXR Cardiac catheterization
Pulmonary • Primary respiratory failure (eg, COPD, asthma) • Large airway obstruction	CXR Blood gas CT angiography of chest Peak and plateau pressures Bronchoscopy
Trauma • Exsanguination • Pneumothorax (rib/sternal fractures) • Cardiac tamponade • Solid organ laceration	Point-of-care ultrasonography Comprehensive cross-sectional imaging (CT chest/abdomen/pelvis) CXR
Neurologic • Stroke • Subarachnoid hemorrhage	CT head CT angiography head/neck CT perfusion
Septic shock	Cultures (blood, urine, ±sputum) CXR Complete blood count Lactate
Metabolic derangements • Diabetic ketoacidosis • Hypoglycemia • Hyperkalemia	Comprehensive metabolic panel
Exposures • Toxicologic • Environmental (eg, electrocution, hypothermia)	Detailed history Urine drug screen (eg, ethanol level, acetaminophen) ECG for intervals

Abbreviations: BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CXR, chest radiograph; ECG, electrocardiogram; RV, right ventricle.

Because cardiovascular causes are common, an electrocardiogram (ECG) should be obtained on all patients after arrest. Although the data on emergent cardiac catheterization postarrest are mixed (discussed later), patients with ACSs and survivable neurologic injury likely benefit from early revascularization.[5] Laboratory testing, including a comprehensive metabolic panel, troponin, lactate, arterial blood gas, glucose, complete blood count, and coagulation studies, should be obtained. Severe metabolic disarray, such as hyperkalemia, diabetic emergencies, and hypoglycemia, can result in arrest. Point-of-care ultrasonography may inform initial resuscitation efforts and narrow the differential diagnosis.[6,7]

Chest radiograph can help with endotracheal tube placement and rule out a pneumothorax. In patients with coma or abnormal neurologic findings, early postarrest computed tomography (CT) imaging of the brain obtained in the ED is abnormal in 5% to 10% of patients.[8] Abnormalities include early cerebral edema, an ominous prognostic sign, and acute cerebrovascular disorder responsible for the initial arrest. Chest compressions commonly result in rib or sternal fractures and associated pneumothorax or solid organ injury.[9] For this reason, many centers obtain comprehensive cross-sectional imaging to screen for both causes and consequences of OHCA. Chest imaging is also sensitive and specific for diagnosis of pulmonary embolism (PE).[10] Arrest from PE defines the embolism as high risk, and these patients should be considered for thrombolytic therapy.[11]

Preventing Early Rearrest

One in 5 patients with OHCA that regain pulses rearrest, and rearrest worsens survival.[12–14] The timing is biphasic, occurring both minutes after ROSC and then hours later. Early rearrest can occur when patients shocked out of ventricular fibrillation refibrillate, particularly in the setting of ongoing myocardial ischemia. These patients may benefit from antidysrhythmic agents such as amiodarone or lidocaine. Refractory ventricular arrhythmias can be managed with mechanical circulatory support and coronary revascularization.[15] Recurrence of pulseless electrical activity is also common as bolus dose vasopressors given during cardiopulmonary resuscitation (CPR) are cleared. Administration of vasoactive agents by continuous infusion is commonly needed in the minutes after initial resuscitation. Patients with cardiogenic shock may require inotropic support.[16–18] The median time to delayed rearrest is about 5 hours.[14] Delayed rearrest often results from persistent myocardial dysfunction,[19] systemic inflammation with associated vasoplegia, and multisystem organ failure.[19,20]

Percutaneous Coronary Intervention

Patients with ST-elevations on ECG postarrest require immediate coronary angiography.[5,21–23] High doses of vasopressors, particularly bolus administration during CPR, can cause transient coronary vasospasm and result in a variety of ECG abnormalities, including ST elevation. It is reasonable to obtain a repeat ECG a few minutes after ROSC because many abnormalities rapidly resolve, but cardiac catheterization should typically not be delayed to obtain serial ECGs over time. Centers capable of performing early neurologic risk stratification may consider deferring percutaneous coronary intervention (PCI) in patients with early objective evidence of severe brain injury, because these patients are unlikely to benefit from revascularization.[24] However, given the limited specificity of many early neuroprognostic signs,[25] these decisions should be made with the utmost caution and only by clinicians with special expertise. Public reporting of postprocedural mortality may create a perverse disincentive to offer PCI to critically ill patients, including those resuscitated from OHCA.[26] Medical

decision making should optimize care for the individual patient rather than reflecting fear of publicly reported outcomes.

Timing of PCI for patients with OHCA without ST-elevations is controversial. Post-arrest ECG is neither sensitive nor specific for diagnosis of ACS.[27–29] For patients with ACS, revascularization can improve myocardial function and prevent recurrent arrhythmias. Nevertheless, a recent randomized controlled trial failed to find benefit from emergent versus delayed PCI in patients with OHCA without ST-elevations.[30] The overall incidence of culprit lesions was only 15% in this study, reflecting the low incidence of cardiac causes of OHCA in patients who survive to the hospital. Other limitations to the study include delayed initiation of targeted temperature management (TTM) and hemodynamic resuscitation, and lack of baseline risk stratification of neurologic illness.

Overall, if pretest probability for ACS is high based on available data and there are neither contraindications to anticoagulation nor evidence of devastating primary brain injury, early PCI should be considered in discussion with interventional cardiology.

Mechanical Circulatory Support

Use of mechanical circulatory support (MCS) during and after cardiac arrest is steadily increasing.[31,32] MCS can preserve brain and coronary perfusion, buying time for definitive treatment in the event of refractory cardiac arrest. After initial ROSC, MCS can augment or replace inadequate cardiac output and may offer myocardial protection in some settings.[33]

Initiating MCS during CPR (termed extracorporeal CPR [ECPR]) requires venoarterial (VA) extracorporeal membrane oxygenation (ECMO). In the event of refractory ventricular arrhythmias from ACS, VA-ECMO can maintain cerebral perfusion and act as a bridge to coronary revascularization.[34] In the event of massive PE or other causes of acute right ventricular failure, VA-ECMO bypasses the failing right ventricle and pulmonary circulation to maintain systemic perfusion. Use of ECPR is growing worldwide.[35] Institutional protocols, inclusion criteria, and outcomes of ECPR vary widely across centers and regions.[34,36–40] ECPR is an expensive and complex intervention with little high-level evidence supporting its use. Nevertheless, it has reasonable face validity and future randomized trials may show benefit.[41]

ECMO may also be useful in the early postarrest period. VA-ECMO provides biventricular and pulmonary support, so it may have a role in both left and right ventricular failure or refractory hypoxemia. Compared with other MCS devices, VA-ECMO is also the most invasive and has the highest associated procedural risks.[35] Intra-aortic balloon pumps (IABPs) and Impella catheters can also be used in the postarrest period to support patients with significant cardiogenic shock. Despite the physiologic rationale for IABP, among patients with cardiogenic shock from acute myocardial infarction, IABP does not improve outcomes compared with conventional care.[42] In addition, it is unclear whether Impella confers significant outcome benefit compared with IABP or conventional care for patients with cardiogenic shock.[43,44]

Preventing Secondary Brain Injury

Anoxic brain injury is the most common proximate cause of death and disability for patients admitted after OHCA.[45–48] The brain is highly susceptible to ischemia after cardiac arrest. Hypoxic ischemic injury can lead to impaired cerebral autoregulation, cerebral edema, and delayed neurodegeneration.[19] Secondary brain injury can occur in the hours to days following ROSC and worsens outcomes.

Optimal perfusion pressure

Adequate cerebral perfusion is necessary after cardiac arrest to prevent further neuronal damage in the already-injured brain. Hours to days after ROSC, cerebral hypoperfusion can develop.[49] During this time, cerebral autoregulation is often impaired, and a smaller decrease in mean arterial pressure (MAP) can cause drastic changes to cerebral blood flow, with critical opening pressures for the cerebral vasculature exceeding 110 mm Hg.[50] Thus, even in the absence of systemic hypotension, cerebral perfusion may be inadequate.[51,52] The ideal MAP after cardiac arrest is unknown and likely needs to be tailored to patient-specific parameters. Multiple observation studies have shown improved neurologic outcome with maintaining a higher MAP (>80 mm Hg), even if vasopressors are required.[53–55] Two recent randomized control trials comparing an MAP of 65 to 75 mm Hg with 80 to 100 mm Hg showed that higher MAPs were feasible but not associated with secondary outcomes of favorable neurologic status.[56,57] One concern about augmenting postarrest MAP is the potential to decrease cardiac output if there is concomitant myocardial dysfunction. Our local practice is to maintain MAPs greater than 80 mm Hg, if other organ systems are not harmed. In any event, hypotension should be avoided.

The best method used to maintain adequate MAP is also unknown. Fluid resuscitation may be required initially and depends on the clinical scenario and the patient's current volume status. Vasopressor or inotropic medications are also often necessary, but the selection of vasoactive agents depends on the type of underlying shock. There is growing literature suggesting potential for harm when epinephrine infusions are used in patients with cardiogenic shock.[58,59]

Ventilator management: oxygenation and ventilation

Hypoxia is consistently associated with worse outcomes after cardiac arrest.[60] Hyperoxia may also cause secondary brain injury, likely mediated by oxidative stress during reperfusion.[61,62] The optimal range for partial pressure of arterial oxygen (Pao_2) is unknown, but 80 to 200 mm Hg is reasonable and a Pao_2 greater than 300 mm Hg should be avoided. If cooling is ongoing, blood gas results must be temperature corrected.

Cerebral blood flow can be altered through ventilation.[21] Hyperventilation-induced hypocapnia causes cerebral vasoconstriction and can cause cerebral ischemia and secondary brain injury.[63] Mild therapeutic hypercapnia can improve cerebral blood flow and may reduce biomarkers of brain injury,[64] although early-phase trial data are mixed.[56] Cerebral vasodilation also increases cerebral blood volume, which can increase intracranial pressure and worsen ischemia.[65] Current guidelines recommend normocapnia ($Paco_2$ 35–45 mm Hg) in the postarrest period.[5,21]

Targeted temperature management

TTM likely offers neuroprotection after cardiac arrest.[5,21,66] The optimal target temperature is unknown. Earlier trials showed benefit from cooling to 32°C to 34°C compared with either normothermia or no temperature management.[67,68] Subsequently, the large TTM trial showed no difference between 33°C and 36°C.[69] These studies enrolled only or mostly patients with initial shockable rhythms. The TTM study was also limited by a lack of standardization of cooling protocols and used a noninferiority trial design.[69] More recently, a smaller randomized controlled trial showed benefit of cooling to 33°C compared with 37°C for patients with an initial nonshockable rhythm.[70] Fever after cardiac arrest must be avoided; each degree more than 37°C is associated with worse outcome.[71]

TTM should be started immediately, because delays can reduce the benefit of cooling. Timing of TTM initiation must be balanced with need for any lifesaving diagnostic

work-up or interventions (eg, PCI) and any contraindications (eg, uncontrolled hemorrhage). The best method for induction is unknown.

Shivering secondary to cooling can result in inability to meet temperature goals, so pharmacologic (sedation with or without neuromuscular blockade) and nonpharmacologic (skin counterwarming) interventions may be necessary. If sedation is required, short-acting medications (fentanyl, propofol, or dexmedetomidine) are preferable, and benzodiazepines should be avoided if possible.[72]

Seizures

Many patients who remain comatose after ROSC have abnormal electroencephalogram (EEG) patterns on the spectrum of seizure activity.[73,74] Seizures may worsen secondary brain injury. However, currently there is little evidence that treating these patterns improves neurologic outcomes.[75] It is reasonable to treat patients after cardiac arrest who have generalized tonic-clonic seizures with antiepileptic drugs, although generalized tonic-clonic seizures are an uncommon manifestation of global anoxic injury.[76] Myoclonus can be observed clinically in the first hours following ROSC, and was historically thought to be ominous. More recent research shows that its presence does not invariably predict poor outcome.[77,78] EEGs can differentiate myoclonus subtypes associated with poor outcome from those that are not ominous.[79,80] Transfer to a center with EEG monitoring should be considered to evaluate for seizures and for prognostication purposes.

Transfer to Specialty Care Center

For resuscitated patients who remain comatose, early transfer to a high-volume specialty care center should be considered.[1] Transport to a cardiac resuscitation center has been associated with increased survival and improved short-term and long-term outcomes.[81–85] These specialty care centers can offer PCI, cardiac and neurologic critical care, and TTM. For unstable patients, active engagement of a critical care transport team is crucial when arranging interfacility transport. Using a critical care transport team has been shown to be safe and feasible.[60] Both secondary prevention (arrhythmia work-up with defibrillator implantation, medication-assisted treatment of opioid addiction) and rehabilitation (neurologic and cardiac) have contributed to better outcomes for cardiac arrest survivors,[86] supporting the importance of transfer to a specialty care center.

Delayed Neuroprognostication

Clinical nihilism and early limitations in care may result in avoidable mortality.[47,48] Overall, quality in post–cardiac arrest neuroprognostication studies is low, and no single sign, symptom, or diagnostic test can accurately predict poor neurologic outcome in the first 24 hours.[25] Validated risk stratification tools exist but are not intended to rule out recoverable disease.[87] Early brain imaging can aid with risk stratification and prognostication but should not be used as a single modality of prognosis in the immediate scenario.[8,88,89] More advanced neuroprognostication tools, such as EEG, MRI, and blood biomarkers, are less useful in the acute postresuscitation period. When the prognosis is unclear, as is common in the acute phase of postarrest care, resuscitation should continue and early withdrawal of life-sustaining therapy should be avoided.

SUMMARY

Postarrest care that improves survival and functional status starts in the prehospital setting and continues to discharge planning. In the ED, parallel postresuscitation

efforts should focus on work-up of underlying causes, preventing rearrest, and minimizing secondary brain injury.

DISCLOSURE

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